Copy of Bill Farland's presentation
ORD/OSWER/OW meeting - November 19, 1999

Update on Perchlorate Assessment Issues

19 November 1999

IPSC

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Outline

- Brief background review
  - Why we are here
  - Perchlorate: What it is, where, & why
  - History of events and IPSC partnership
- Assessment and peer review status
  - Mode of action framework
  - Human toxicology
- Regulatory status
- Future developments / timeline
- "Eco Summit" priorities

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OSWER / OW Concerns Why We are Here

- Perchlorate assessment schedule slippage
- Inference that ORD is @ fault
- Suggestion that "RfD" could be generated by March 2000
- Concerns reflect regulatory pressure from States and Regions (?)

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What is Perchlorate?

- Primary oxidizer in solid rockets
  - Army, Navy, Air Force, NASA
    - Titan, Minuteman, Peacekeeper, Hawk, Polaris, Space shuttle boosters
- Other sources include air bags, fireworks, and some fertilizers
- Anion (ClO_4^-) exists as a contaminant in ground and surface waters from dissolution of various solid salts
- Persistent for many decades under typical ground and surface water conditions

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Perchlorate "Where it's at" in 11/99

- MDL @ 4 ppb since 4/97; EPA Std. Method 309 for detection in water @ same level due in a few months
- Currently 14 states with confirmed contamination
- AP manufacturers or users in 44 states based on responses to EPA Information Requests

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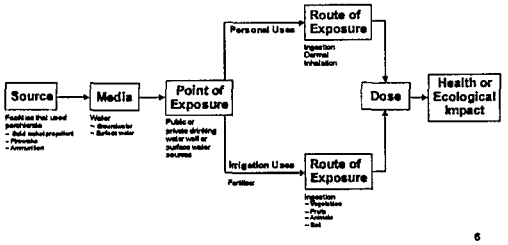
Goal: Comprehensive Characterization of Perchlorate Contamination



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Assessment History

- **Expert peer review in 3/97 of an "RfD" presented by TERA; same basis as provisional RfD values from Superfund Technical Support Center in NCEA underlying existing provisional guidance levels of 4 – 18 ppb**
- **Panel concluded 1997 data base inadequate for RfD derivation**
- **Available mechanistic insights suggested alternative testing strategy**
- **Eight (8) additional new categories of studies recommended and funded**

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1997 Recommended Studies*

- 90-Day subchronic bioassay (rats)
- Developmental neurotoxicity study (rats)
- Genotoxicity assays (Salmonella, MN, lymphoma)
- Mechanistic studies
- ADME - Absorption, Distribution, Metabolism and Elimination
- Developmental study (rabbits)
- 2-Generation reproductive toxicity study (rats)
- Immunotoxicity (mice)

* Hormone analyses (T4, T3, and TSH), thyroid histopathology, and recovery satellites also added

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Interagency Perchlorate Steering Committee (IPSC) Pro-Active Problem Solving

- **Formed in January 1998**
- **Facilitates and coordinates accurate accounts of technical issues and areas of concern**
- **Subcommittee devoted to each critical area (health; analytical; treatment tech; eco / transport / transformation; tech transfer / communication)**
- **Membership by Fed, tribal, state and local governments (currently 23 Agencies)**
- **Meetings open to public**
- **Coordinated with AWWARF**

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EPA Assessment

Unique Attributes

- Partnership to develop data base
- Both human and ecological risk assessments of available data
- Harmonized approach to noncancer and cancer toxicity based on mode of action

Process

NCEA published external peer review draft in December 1998
Peer Review Panel held February 1999

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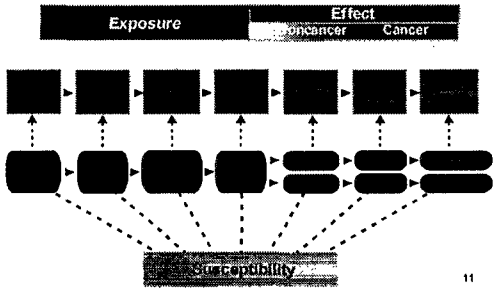
Figure 8. Proposed Mode-of-Action Model for Risk Assessment of Perchlorate



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Health Assessment Status

- Hormone and histology results support proposed mode-of-action model; applauded by External Peer Review Panel (Feb 99)
- Uncertainties to be better addressed by recommended studies (pending):
  - Normalization of nomenclature and severity scoring of histopathology across studies
    - NTP Pathology Working Group
    - Both thyroid and brain sections
  - Inter-laboratory validation study of hormone analyses to decrease variability

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Health Assessment Status

- Uncertainties to be better addressed by recommended pending studies (continued):
  - "Effects" protocol to evaluate thyroid and brain at critical developmental time points; evaluate fetal anomalies per OPPTS 870.3700 in rats
  - Repeat of motor activity studies in pups due to variability; ascertain effect level
  - Repeat of immunotoxicity SRBC assays due to *deficiencies; recommended new delayed type* hypersensitivity (DTH) assay (LLN)
  - Kinetics of perchlorate iodide uptake inhibition and hormone analyses in humans; PK in pregnant and lactating dams, and fetuses at various time points

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Health Assessment Status
Events Sequence Since Feb 99

- Procure additional funding
  - EPA / NIEHS
  - DoD
  - NASA
  - Perchlorate Study Group (PSG)
- Protocol development, review, and implementation
  - Cost estimation
  - Approval
  - Award

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Health Assessment Status
Funding Procurement & Protocol Implementation

- EPA / NIEHS:
  - PWG for thyroids and brains: ORD "IOU" through existing contracts
  - Target originally Aug 1999 then Nov 1999
  - Thyroid PWG Status: January 2000
    - Due to delays in inventory and materials provided by contracting laboratories and need for additional days to convene review of extensive inventory
  - Brain PWG Status: Postponed due to review noting inadequacy of existing slides -- awaits data from "effects" protocol (June 2000)

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Health Assessment Status
Funding Procurement & Protocol Implementation

- **DoD / NASA: Significant investment to date ("pay me now or pay me later")**
  - USAF ($1.5M)
  - NASA ($350K)
- **June briefing with NCEA to DoD Environment, Safety and Occupational Health Policy Board**
- **Oct 99 letter from Under Secretary of Defense for Environmental Security tapping tri-services for additional $FY99 and $FY00: USAF ($300K); USN ($1.4M) and USA ($650K)**

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Health Assessment Status
Funding Procurement & Protocol Implementation

- **DoD / NASA:**
  - **Analytical hormone analyses for various studies:**
    - Inter-laboratory validation report
      - Cost: $40K
      - Due date: Jan 2000
    - Other studies: Immunotoxicity (PSG); "effects protocol" (PSG); motor activity (USN); PK studies
  - **Motor activity in pups repeat study (USN)**
    - Cost: $ 100K
    - Due date: June 2000

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Health Assessment Status
Funding Procurement & Protocol Implementation

- **DoD / NASA:**
  - Adult Rat PK study and model (underway)
    - Cost: $150K
    - Due date: March 2000
  - Pregnant / lactating females / pups PBPK study and model
    - Cost: $200K
    - Due date: First data in March 00; model in Jun - Aug 00
  - Human PK data and Model Phase I (preliminary)
    - Cost: $50K
    - Due date: March 00
  - Human PK Model Phase II (validation)
    - Cost: $ 50K
    - Due date: June 00 pending data availability from PSG

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Health Assessment Status

Funding Procurement & Protocol Implementation

- PSG ($1.4 to date, additional $1.4M committed)
  - Repeat immunotoxicity studies (SRBC, DTH):
    - $30K
    - *Due date: May 2000*
  - "Effects" protocol:
    - $450K
    - Due date: June 2000
  - Human repeated (14-day) PK study in humans:
    - Protocol development completed with AFRL and NCEA
    - $? On bid
    - Due date: June 2000
  - Human short-term low-dose PK study:
    - $150K
    - Due date: Phase I completed; Phase II underway (June 2000)

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Revised Harmonized Oral Human Health Benchmark ("RfD")

- Data across comprehensive array of endpoints to establish target tissue
- Mechanistically-motivated special studies to characterize critical dose-response relationships
- Harmonized nonlinear approach to both cancer and noncancer assessment based on mode of action
- New "RfD" estimate at 0.0009 mg/kg-day translates to approximately 2-fold higher guidance level (32 ppb)
- Future refinements with new data, PWG results, and development of PBPK dosimetry model
- Due to these remaining uncertainties, ORD has recommended that original RfD range of 0.0001 to 0.0005 mg/kg-day be used in interim

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Health Assessment Development Process Continued Improvement

- Review of additional pending data (Ongoing)
- Response / revisions subsequent to external peer review final report (Fall 1999)
- Pathology Working Groups (Jan 2000 / June 2000)
- Comprehensive PBPK model (June 2000)
- Additional internal peer review (September 2000)
- Additional external peer review (Fall 2000)
- Submit final revised assessment to Integrated Risk Information System (IRIS) process (Jan 2001)

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Perchlorate Regulatory Status

- No National Primary Drinking Water Regulation (NPDWR)
- No site-specific cleanup guidance levels
- Public comment placed on OGWDW Contaminant Candidate List (CCL) in March 1999
  - **Research (Health, Analytical, Treatment) and Occurrence Priority**
  - ***Determination to regulate not likely by 2001***
- ORD guidance issued in June 1999
- Included on Unregulated Contaminant Monitoring Regulation (UCMR) August 31, 1999

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Perchlorate Regulatory Status

- Near Term (1 to 2 years): Use "RfD" to develop a health advisory (HA) under SDWA general authority
  - Not federally enforceable and subject to change
  - Technical guidance to assist State, Tribal and local officials responsible for public health
- Longer Term (3 to 5 years): Data gaps filled and perchlorate moves to the regulatory determination category of next CCL in 2003; MCL?
- OSWER, States, and Regions: Develop own guidance levels based on available information until NPDWR available

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Comprehensive Characterization Status 11/99

- Health and ecotoxicology assessment estimates required as focal points of integrated approach
- Indirect exposure pathway important to determine background, relative source contribution
- Extension of analytical method now required to other matrices (soil, plant & animal tissues)
- Risk characterization precluded by accurate exposure surveys
- Treatment technology will be final frontier (DoD budgeting $3M / yr. for next 3 years)

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Screening Ecological Assessment

- Limited in scope due to the set of data that could be generated in short time frame
- Scope nevertheless responsive to stakeholder concerns regarding lettuce
- Problem formulation focused on selection of assessment endpoints, derivation of conceptual model, and analysis
- Analysis revealed uncertainties and research needs identified to guide next tier of testing
- "Eco summit" held on Earth Day 1999 at Little Rock AFB to address peer review recommendations

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"Eco Summit" Priorities Bioaccumulation

- Steady-state and mass balance
- Representative of growing season (harvest) for critical crops
  - EPA-NERL preliminary data on uptake from fertilizers in leaf lettuce and Indian mustard into leaves, stems, and roots (approximately 0.001 wt%)
  - Lettuce seedlings grown in water only (hydroponic) for 24 days suggest potential for accumulation
- Representative of farming practices / soil conditions
  - Preliminary EPA-NERL characterization of adsorption characteristics of perchlorate in soils indicates pH and concentration dependence

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"Eco Summit" Priorities "Farm Gate" Analyses ($250K)

- Lettuce, soybean, corn, milk, oranges, melons, tomatoes, peppers, wheat
  - "860" OPPT guidance re: crop residues
  - Analytical methods
    - Interlaboratory "round robin" report on fertilizer samples (AFRL, EPA-NERL, Industry, TFI) due January 1999 will address source and method variability, interference, etc.
    - TFI developing new round robin protocol in collaboration with AFRL, EPA, USDA to address agricultural practice; due June 2000
    - Preliminary data indicate concentrations in range of 0.2 to 0.8 wt %
    - Development and validation of method extension to plant and animal tissues

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"Eco Summit" Priorities
Site-Specific Analyses ($250K)

- Located @ Lake Mead/LV Wash, Indian Head, Lower Colorado, McGregor, White Sands
  - Known sites of concern; also representative of various soil types and climate considerations
  - Soil, water, tissues concentrations / mass balance
  - Analytical needed for soil, water, tissues
  - Soil composition / other anions / background
  - Sampling strategy / other sources

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"Eco Summit" Priorities
Other Eco / Xport / Xform Issues

- Phytoremediation (U of Georgia for USAF)
- Toxicity testing and sampling for other receptors on ecosystem CSM
  - Brooks AFB (chronic Hyallela, Pimephales, Selenastrum; Medaka fish embryo assay)
  - Field mice (Texas Tech University for USAF)
  - Embryonic toxicology in amphibians (U of Oklahoma for USAF)
- Soil column studies (NERL-Athens for USAF)
- Literature searches
  - EPA OERR
  - AFRL

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The Perchlorate Contamination Challenge

Credible Science

Credible Decisions

- Accurate risk characterization
- Appropriate management strategies

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